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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/497,997	02/04/2000	Theresa Ternynck	0660-0166-OX-CONT	8156

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EXAMINER
BROWN, STACY S

ART UNIT	PAPER NUMBER
1648	24

DATE MAILED: 07/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/497,997	TERNYNCK ET AL.	
	Examiner	Art Unit	
	Stacy S Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-67* is/are pending in the application.

4a) Of the above claim(s) *21-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-58 and 60-67* is/are rejected.

7)☒ Claim(s) *59* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment received March 11, 2002 is acknowledged and entered. Claims 1-20 are cancelled and new claims 45-67 are added. Claims 21-67 are pending. Claims 21-44 are withdrawn from consideration being drawn to non-elected inventions. Claims 45-67 are examined.

2. The objections to the abstract and claims are moot in view of Applicant's amendments. The rejections under 35 U.S.C. 101, 102(b), 103(a) and 112, second paragraph, are moot in view of Applicant's amendments. This action is non-final because new grounds of rejection are made.

Specification

3. It is noted that Applicant's specification lacks titles for elements (b) and (e) through (h) below. As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading.

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.
(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino

acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Claim Objections

4. Claims 59, 63 and 66 are objected to because:

- Claim 59 contains non-elected sequences (SEQ ID NOS: 2 and 3). *The original election of SEQ ID NO: 1 was not a species election, rather, it was a restriction. The claim should not recite non-elected inventions.*
- Claims 63 and 66, line 2, after "selected" are missing "from".
- Claim 67 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 64. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 45-58, 60-63 are rejected under 35 U.S.C. 102(a) as being anticipated by Avrameas *et al* (*PNAS USA*, 1998). The claims are drawn to an isolated polypeptide comprising a unique or repeated peptide motif, which penetrates into a cell. The polypeptide can be an antibody fragment from the hypervariable region, heavy chain, CDR2, CDR3 or a fusion between CDR3 and CDR2. The fragment is from a polyreactive or penetrating antibody and can be up to 100 amino acids. It can have a lysine amino acid region and binds DNA *in vitro*.

Avrameas teaches polyreactive and penetrating anti-DNA monoclonal antibodies and functional fragments thereof with lysine residues that can penetrate cells (abstract and page 5604, column 2). The fragments were 30-amino acid peptides having CDR2 and CDR3 of the heavy chain variable region (abstract). Peptide libraries were used to find antibodies that penetrate cells (page 5603, col. 1). Avrameas' polypeptide anticipates the polypeptide in claims 45-58, 60-63.

7. Claims 45-52, 56-58, 60-63 are rejected under 35 U.S.C. 102(a) as being anticipated by Weisbart (WO 97/32602). The claims are summarized above.

Weisbart teaches penetrating anti-dsDNA antibodies and Fab fragments thereof with lysine residues that can penetrate cells (abstract and page 7, lines 23-25). By definition, Fab fragments have CDR2 and CDR3 of the heavy chain variable region. Although Weisbart is silent on obtaining the polypeptide by screening a library, the claim is still anticipated because it is a product-by-process claim. Weisbart's polypeptide anticipates the polypeptide in claims 45-58, 60-63.

8. Claims 45-52, 56-58, 60-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Zack *et al* (*J. Immunology*, 1996). The claims are summarized above.

Zack teaches penetrating anti-dsDNA autoantibodies and Fab fragments thereof with lysine residues that can penetrate cells (abstract and page 2087, col. 1, paragraph 3). By definition, Fab fragments have CDR2 and CDR3 of the heavy chain variable region. Although Zack is silent on obtaining the polypeptide by screening a library, the claim is still anticipated because it is a product-by-process claim. Zack's polypeptide anticipates the polypeptide in claims 45-58, 60-63.

Claim Rejections - 35 USC § 103

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 45-58 and 60-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Avrameas *et al*, as applied to claims 45-58, 60-63 and further in view of Jin et al (*PNAS USA* Vol. 94:14683-14688 (1997)) and Weisbart. The claims are summarized above. Also claimed is a polypeptide that binds heparin *in vitro*. Avrameas is silent on heparin.

Heparin is well known in the art, as evidenced by Jin. Jin teaches that heparin is the initial-choice anticoagulant for treating thromboembolic disease (abstract). It would have been obvious to use Avrameas' polypeptide to deliver heparin because it is the drug of choice for many patients suffering from thromboembolic disease. One would have been motivated to incorporate heparin into the drug-delivery method of Avrameas because the method is for the intracellular delivery of proteins and genes (abstract). One would have had a reasonable

expectation of success that heparin could be administered via Avrameas' polypeptide given Weisbart's teaching that antibody fragments can deliver many types of biologically active materials (page 5, lines 7-18).

10. Claims 45-58 and 60-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weisbart or Zack as applied to claims 45-58 and 60-63 above, and further in view of Avrameas and Jin. The claims are summarized above. Weisbart and Zack are silent on the length of the polypeptides and the binding to heparin.

Avrameas teaches fragments of 30-amino acids having CDR2 and CDR3 of the heavy chain variable region (abstract).

Heparin is well known in the art, as evidenced by Jin. Jin teaches that heparin is the initial-choice anticoagulant for treating thromboembolic disease (abstract). The reasons for obviousness over Jin are summarized above.

It would have been obvious to incorporate the characteristics of Avrameas' polypeptide into the polypeptides of Weisbart or Zack. One would have been motivated because both polypeptides are anti-DNA fragments of penetrating antibodies, useful for delivering molecules into cells. One would have had a reasonable expectation of success that if Weisbart or Zack's polypeptide were 30 amino acids in length, it would be functional because Avrameas' similar polypeptide penetrates cells.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

11. Claim 59 is free of the prior art.

Papers relating to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 located in Crystal Mall 1. The Fax number for Art Unit 1648 is (703) 308-4426. All Group 1600 Fax machines will be available to receive transmissions 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30, (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stacy S. Brown, whose telephone number is (703) 308-2361. The Examiner can normally be reached on Monday through Friday and alternate Wednesdays from 6:30 AM-4:00 PM, (EST). If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, James C. Housel, can be reached at (703) 308-4027. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stacy S. Brown
July 12, 2002

ANKYEL T. PARK, PH.D
PRIMARY EXAMINER